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FILE 'BIOSIS' ENTERED AT 08:47:45 ON 16 SEP 2005
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L1          20 DPPIV AND (INSERTION OR ADDITION OR EXTENSION) AND AMINO
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L2   ANSWER 1 OF 13  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
ACCESSION NUMBER:    2005:160164  BIOSIS
DOCUMENT NUMBER:     PREV200500158467
TITLE:               Aminopeptidases and dipeptidyl-peptidases secreted by the
                     dermatophyte Trichophyton rubrum.
AUTHOR(S):           Monod, Michel [Reprint Author]; Lechenne, Barbara; Jousson,
                     Olivier; Grand, Daniela; Zaugg, Christophe; Stocklin, Reto;
                     Grouzmann, Eric
CORPORATE SOURCE:    Serv Dermatol and Venerol, Ctr Hosp Univ Vaudois, Lausanne,
                     Switzerland
                     Michel.Monod@chuv.hospvd.ch
SOURCE:              Microbiology (Reading), (January 2005) Vol. 151, No. Part
                     1, pp. 145-155. print.
                     ISSN: 1350-0872 (ISSN print).
DOCUMENT TYPE:       Article
LANGUAGE:            English
OTHER SOURCE:        DDBJ-AF407232; EMBL-AF407232; GenBank-AF407232;
                     DDBJ-AY496929; EMBL-AY496929; GenBank-AY496929;
                     DDBJ-AY496930; EMBL-AY496930; GenBank-AY496930;
                     DDBJ-AY497021; EMBL-AY497021; GenBank-AY497021
ENTRY DATE:          Entered STN: 27 Apr 2005
                     Last Updated on STN: 27 Apr 2005
AB   The nature of secreted aminopeptidases in Trichophyton rubrum was
     investigated by using a reverse genetic approach.  T rubrum, genomic and
     cDNA libraries were screened with Aspergillus spp. and Saccharomyces
     cerevisiae aminopeptidase genes as the probes.  Two leucine
     aminopeptidases, ruLap1 and ruLap2, and two dipeptidyl-peptidases, ruDppIV
     and ruDppV, were characterized and compared to orthologues secreted by
     Aspergillus fumigatus using a recombinant protein from Pichia pastoris.
     RuLap1 is a 33 kDa nonglycosylated protein, while ruLap2 is a 58-65 kDa
     glycoprotein.  The hydrolytic activity of ruLap1, ruLap2 and A. fumigatus
     orthologues showed various preferences for different aminoacyl-7-amido-4-
     methylcoumarin substrates, and various sensitivities to inhibitors and
     cations. ruDppIV and ruDppV showed similar activities to A. fumigatus
     orthologues.  In addition to endopeptidases, the four
     aminopeptidases ruLap1, ruLap2, ruDppIV and ruDppV were produced by T
     rubrum in a medium containing keratin as the sole nitrogen source.
     Synergism between endo- and exopeptidases is likely to be essential for
     dermatophyte virulence, since these fungi grow only in keratinized
     tissues.

L2   ANSWER 2 OF 13     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2005182735     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15813678
TITLE:               Genes and molecules involved in Aspergillus fumigatus
                     virulence.
AUTHOR:              Rementeria Aitor; Lopez-Molina Nuria; Ludwig Alfred;
                     Vivanco Ana Belen; Bikandi Joseba; Ponton Jose; Garaizar
                     Javier
CORPORATE SOURCE:    Departamento Inmunologia, Microbiologia y Parasitologia,
                     Facultad de Ciencia y Tecnologia, Universidad del Pais
                     Vasco, Spain.. oiprerua@lg.ehu.es
```

SOURCE: Revista iberoamericana de micologia : organo de la Asociacion Espanola de Especialistas en Micologia, (2005 Mar) 22 (1) 1-23. Ref: 213
Journal code: 9425531. ISSN: 1130-1406.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20050408
Last Updated on STN: 20050608
Entered Medline: 20050607

AB Aspergillus fumigatus causes a wide range of diseases that include mycotoxicosis, allergic reactions and systemic diseases (invasive aspergillosis) with high mortality rates. Pathogenicity depends on immune status of patients and fungal strain. There is no unique essential virulence factor for development of this fungus in the patient and its virulence appears to be under polygenetic control. The group of molecules and genes associated with the virulence of this fungus includes many cell wall components, such as beta-(1-3)-glucan, galactomannan, galactomannanproteins (Afmp1 and Afmp2), and the chitin synthetases (Chs; chsE and chsG), as well as others. Some genes and molecules have been implicated in evasion from the immune response, such as the rodlets layer (rodA/hyp1 gene) and the conidial melanin-DHN (pksP/alb1 gene). The detoxifying systems for Reactive Oxygen Species (ROS) by catalases (Cat1p and Cat2p) and superoxide dismutases (MnSOD and Cu, ZnSOD), had also been pointed out as essential for virulence. In addition, this fungus produces toxins (14 kDa diffusible substance from conidia, fumigaclavin C, aurasperon C, gliotoxin, helvolic acid, fumagilin, Asp-hemolysin, and ribotoxin Asp fI/mitogilin F/restrictocin), allergens (Asp f1 to Asp f23), and enzymatic proteins as alkaline serin proteases (Alp and Alp2), metalloproteases (Mep), aspartic proteases (Pep and Pep2), dipeptidyl-peptidases (DppIV and DppV), phospholipase C and phospholipase B (Plb1 and Plb2). These toxic substances and enzymes seems to be additive and/or synergistic, decreasing the survival rates of the infected animals due to their direct action on cells or supporting microbial invasion during infection. Adaptation ability to different trophic situations is an essential attribute of most pathogens. To maintain its virulence attributes A. fumigatus requires iron obtaining by hydroxamate type siderophores (ornitin monooxigenase/SidA), phosphorous obtaining (fos1, fos2, and fos3), signal transductional falls that regulate morphogenesis and/or usage of nutrients as nitrogen (rasA, rasB, rhbA), mitogen activated kinases (sakA codified MAP-kinase), AMPc-Pka signal transductional route, as well as others. In addition, they seem to be essential in this field the amino acid biosynthesis (cpcA and homoaconitase/lysF), the activation and expression of some genes at 37 degrees C (Hsp1/Asp f12, cgrA), some molecules and genes that maintain cellular viability (smcA, Prp8, anexins), etc. Conversely, knowledge about relationship between pathogen and immune response of the host has been improved, opening new research possibilities. The involvement of non-professional cells (endothelial, and tracheal and alveolar epithelial cells) and professional cells (natural killer or NK, and dendritic cells) in infection has been also observed. Pathogen Associated Molecular Patterns (PAMP) and Patterns Recognizing Receptors (PRR; as Toll like receptors TLR-2 and TLR-4) could influence inflammatory response and dominant cytokine profile, and consequently Th response to infec tion. Superficial components of fungus and host cell surface receptors driving these phenomena are still unknown, although some molecules already associated with its virulence could also be involved. Sequencing of A. fumigatus genome and study of gene expression during their infective process by using DNA microarray and biochips, promises to improve the knowledge of virulence of this fungus.

L2 ANSWER 3 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2004496598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15213224
TITLE: Crystal structure of CD26/dipeptidyl-peptidase IV in complex with adenosine deaminase reveals a highly

amphiphilic interface.
AUTHOR: Weihofen Wilhelm A; Liu Jiango; Reutter Werner; Saenger Wolfram; Fan Hua
CORPORATE SOURCE: Institut fur Chemie/Kristallographie, Freie Universitat Berlin, Takustrasse 6, D-14195 Berlin, Germany.
SOURCE: Journal of biological chemistry, (2004 Oct 8) 279 (41) 43330-5. Electronic Publication: 2004-06-22.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1W1I
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20041007
Last Updated on STN: 20041219
Entered Medline: 20041124

AB Dipeptidyl-peptidase IV (**DPPIV** or CD26) is a homodimeric type II membrane glycoprotein in which the two monomers are subdivided into a beta-propeller domain and an alpha/beta-hydrolase domain. As dipeptidase, **DPPIV** modulates the activity of various biologically important peptides and, in **addition**, **DPPIV** acts as a receptor for adenosine deaminase (ADA), thereby mediating co-stimulatory signals in T-lymphocytes. The 3.0-A resolution crystal structure of the complex formed between human **DPPIV** and bovine ADA presented here shows that each beta-propeller domain of the **DPPIV** dimer binds one ADA. At the binding interface, two hydrophobic loops protruding from the beta-propeller domain of **DPPIV** interact with two hydrophilic and heavily charged alpha-helices of ADA, giving rise to the highest percentage of charged residues involved in a protein-protein contact reported thus far. Additionally, four glycosides linked to Asn229 of **DPPIV** bind to ADA. In the crystal structure of porcine **DPPIV**, the observed tetramer formation was suggested to mediate epithelial and lymphocyte cell-cell adhesion. ADA binding to **DPPIV** could regulate this adhesion, as it would abolish tetramerization.

L2 ANSWER 4 OF 13 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004197248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15095403
TITLE: **Amino**-terminal processing of MIP-1beta/CCL4 by CD26/dipeptidyl-peptidase IV.
AUTHOR: Guan Ennan; Wang Jinhai; Norcross Michael A
CORPORATE SOURCE: Division of Therapeutic Proteins, Center for Drug Evaluation and Research, Food and Drug Administration, Bethesda, Maryland 20892, USA.. guan@cber.fda.gov
SOURCE: Journal of cellular biochemistry, (2004 May 1) 92 (1) 53-64.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20040420
Last Updated on STN: 20041220
Entered Medline: 20041216

AB CD26 is a membrane-bound ectopeptidase with dipeptidyl peptidase IV (**DPPIV**) activity that has diverse functional properties in T cell physiology and in regulation of bioactive peptides. We have previously reported that activated human peripheral lymphocytes (PBL) secrete an **amino**-terminal truncated form of macrophage inflammatory protein (MIP)-1beta/(3-69) with novel functional specificity for CCR1, 2, and 5. In this report, we show that the full length MIP-1beta is processed by CD26/**DPPIV** to the truncated form and that cleavage can be blocked by **DPPIV** inhibitory peptides derived from HIV Tat(1-9) or the thromboxane A2 receptor, TAX2-R(1-9). **Addition** of Tat(1-9) or TAX2-R(1-9) peptides to PBL cultures partially blocks endogenous MIP-1beta processing. The kinetics of conversion of MIP-1beta

from intact to MIP-1beta(3-69) in activated PBLs correlates with cell surface expression of CD26. Our results suggest that NH2-terminal processing of MIP-1beta and possibly other chemokines may depend on the balance between CD26/DPPIV enzymatic activity and cellular and viral proteins that modulate enzyme function.

L2 ANSWER 5 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2003068742 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12579300
TITLE: CD26: a novel treatment target for T-cell lymphoid malignancies? (Review).
AUTHOR: Sato Kazuya; Dang Nam H
CORPORATE SOURCE: Department of Lymphoma/Myeloma, UT M.D. Anderson Cancer Center, Houston, TX 77030, USA.
SOURCE: International journal of oncology, (2003 Mar) 22 (3) 481-97. Ref: 123
Journal code: 9306042. ISSN: 1019-6439.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20030212
Last Updated on STN: 20031217
Entered Medline: 20031118
AB CD26 is a surface glycoprotein with intrinsic dipeptidyl peptidase IV (DPPIV) enzyme activity with multiple biological roles, including being intricately involved in immunoregulation as a T-cell activation molecule and as a regulator of chemokine function. T-cell lymphoid malignancies represent a heterogeneous group of diseases that are generally aggressive and are for the most part resistant to current treatment modalities. Previous studies showed that CD26 is expressed on selected T-cell neoplasms, suggesting a potential role for CD26 in tumor development. We review herein recent classification schemes for T-cell lymphoid malignancies that take into account various facets of their clinical presentation. In addition, we discuss findings supporting the conclusion that CD26 has an essential role in human T-cell activation, as well as its ability to regulate the biological effects of selected chemokines through its DPPIV activity. Finally, we will present recent work from our laboratory that indicates a potential role for CD26 as a molecular target for novel treatment modalities for T-cell lymphoid malignancies.

L2 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:356425 BIOSIS
DOCUMENT NUMBER: PREV200300356425
TITLE: Cell Surface Peptidase CD26/DPPIV Regulates CXCL12/SDF-1alpha Mediated Chemotaxis of Sca-1+/c-kit+/lin- Mouse Progenitor Cells In Vitro and G-CSF-Induced Progenitor Cell Mobilization In Vivo.
AUTHOR(S): Christopherson, Kent W. II [Reprint Author]; Cooper, Scott [Reprint Author]; Broxmeyer, Hal E. [Reprint Author]
CORPORATE SOURCE: Microbiology and Immunology, Indiana University School of Medicine, Indianapolis, IN, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 399. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003
AB CD26/DPPIV (dipeptidylpeptidase IV) is a membrane-bound

extracellular peptidase that cleaves dipeptides from the N-terminus of polypeptide chains. The N-terminus of chemokines is known to interact with the extracellular portion of chemokine receptors and removal of these amino acids in many instances results in significant changes in functional activity. CD26/DPPIV has the ability to cleave the chemokine CXCL12/SDF-1alpha at its position two proline. CXCL12/SDF-1alpha induces migration of hematopoietic stem and progenitor cells and it is thought that CXCL12/SDF-1alpha plays a crucial role in mobilization of these cells from the bone marrow. Given that we had previously found CD26/DPPIV expression and activity in a subpopulation of CD34+ cord blood cells (Christopherson KW 2nd, et al. Exp Hematol. 6:83, 2002), we tested Sca-1+lin- cells isolated from mouse bone marrow. Mouse marrow cells were chosen because mice represent a useful model for in vivo mobilization studies. Lin+ cells were depleted using a density particle murine progenitor enrichment cocktail and four-color flow cytometry was then performed on cells by labeling for murine CD26, CXCR4, Sca-1, and c-kit. Sca-1+c-kit-lin- and Sca-1+c-kit+lin- were simultaneously sorted. We found by flow cytometry that CD26/DPPIV is expressed by greater than 75% on Sca-1+c-kit-lin- or Sca-1+c-kit+lin- hematopoietic cells isolated from mouse bone marrow and that these cells have DPPIV activity using the chromogenic substrate Gly-Pro-p-nitoanilide. It was also discovered that CXCR4, the receptor for CXCL12/SDF-1alpha, being expressed in greater than 90% Sca-1+c-kit-lin- or Sca-1+c-kit+lin- cells, is expressed by both the CD26+ and CD26- population of cells. This sets up the potential for CD26/DPPIV to act as a regulator of cellular response to CXCL12/SDF-1alpha. Since, the involvement of CD26/DPPIV in hematopoietic stem and progenitor cell migration had never been previously examined in normal human or mouse bone marrow, chemotaxis assays were performed using sorted Sca-1+c-kit-lin- and Sca-1+c-kit+lin- mouse bone marrow to test the functional role of CD26/DPPIV. Comparison of cell migration induced by the normal CXCL12/SDF-1alpha to the CD26/DPPIV cleaved form, CXCL12/SDF-1alpha(3-68), showed an inability of CXCL12/SDF-1alpha (3-68) to induce the migration of Sca-1+c-kit-lin- or Sca-1+c-kit+lin- mouse marrow cells. In addition, CXCL12/SDF-1alpha(3-68) acts as an antagonist, resulting in the reduction of migratory response to normal CXCL12/SDF-1alpha. Treatment of Sca-1+c-kit-lin- or Sca-1+c-kit+lin- mouse marrow cells with Diprotin A, a specific CD26/DPPIV inhibitor, enhanced the migratory response of these cells to CXCL12/SDF-1alpha by two-fold. Finally, to test for potential in vivo relevance of these in vitro observations, mice were treated with the CD26/DPPIV inhibitor, Diprotin A (5mmol/mouse 2x/day for 2 days), during G-CSF induced mobilization (2.5mg/mouse 2x/day for 2 days). Treatment of mice with Diprotin A during the G-CSF regiment resulted in a reduction in progenitor cells/ml to one-third for CFU-GM, two-thirds for BFU-E, and one-third for GEMM of that observed with the G-CSF regiment alone. This reduction in the number of progenitor cells mobilized suggests that a mechanism of action of G-CSF mobilization involves CD26/DPPIV activity.

L2 ANSWER 7 OF 13 EMBASE
on STN

ACCESSION NUMBER: 2001269893 EMBASE
TITLE: Protein kinase C-dependent distribution of the multidrug resistance protein 2 from the canalicular to the basolateral membrane in human HepG2 cells.
AUTHOR: Kubitz R.; Huth C.; Schmitt M.; Horbach A.; Kullak-Ublick G.; Haussinger D.
CORPORATE SOURCE: Dr. D. Haussinger, Klinik fur Gastroenterologie, Universitat Dusseldorf, Moorenstrasse 5, D-40225 Dusseldorf, Germany. RKubitz@t-online.de
SOURCE: Hepatology, (2001) Vol. 34, No. 2, pp. 340-350.
Refs: 58
ISSN: 0270-9139 CODEN: HPTLD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20010816
Last Updated on STN: 20010816

AB The subcellular localization of hepatobiliary transport proteins directly affects the rate of bile formation, e.g., the conjugate export pump multidrug resistance protein 2 (MRP2) is regulated on a short-term scale by retrieval from and **insertion** into the canalicular membrane in the liver. This study reports on the effects of protein kinase C on MRP2 localization and activity in human hepatoblastoma HepG2 cells. MRP2 was detected in HepG2 cells by immunocytochemistry and Western blot analysis. Functional activity was assessed by confocal laser scanning microscopy using fluorescent MRP2 substrates. In untreated HepG2 cells MRP2 was almost exclusively localized at the apical membrane. Treatment of HepG2 cells with phorbol-12-myristate-13-acetate (PMA) resulted in a rapid decrease of apically localized MRP2 and a loss of more than 90% of pseudo-canaliculi within 4 hours. This was accompanied by a reduced pseudocanalicular secretion of the MRP2 substrate glutathione-methylfluorescein. Interestingly, PMA treatment (1-100 nmol/L) led to the appearance of immunoreactive MRP2 at the basolateral membrane within 30 minutes. This was shown by its colocalization with MRP1, human dipeptidylpeptidase IV (**DPPIV**), and transfected rat Ntcp. The effects of PMA on MRP2 localization were sensitive to the protein kinase C (PKC) inhibitor Go6850 but insensitive to inhibition of MEK by PD098059. Basolateral MRP2-appearance was not inhibited by cycloheximide or by disruption of microtubules or microfilaments. In rat livers cholestasis was induced by PMA (100 nmol) and Mrp2 was detected at the basolateral membrane in some areas, colocalizing with Ntcp. The data suggest that retargeting of canalicular MRP2 to the basolateral membrane due to PKC activation may represent a novel mechanism that may contribute to cholestasis.

L2 ANSWER 8 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2001217320 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11284388
TITLE: Peptide truncation by dipeptidyl peptidase IV: a new pathway for drug discovery?.
AUTHOR: Scharpe S; De Meester I
CORPORATE SOURCE: Laboratory for Medical Biochemistry, University of Antwerp, UIA Universiteitsplein 1, B-2610 Antwerpen.
SOURCE: Verhandelingen - Koninklijke Academie voor Geneeskunde van Belgie, (2001) 63 (1) 5-32; discussion 32-3. Ref: 95
Journal code: 0413210. ISSN: 0302-6469.
PUB. COUNTRY: Belgium
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

AB Membrane peptidases are a group of ectoenzymes with a broad functional repertoire. In protein metabolism, their importance is well known, especially in peptide degradation and **amino** acid scavenging at the intestinal and renal brush border. However, they also perform more subtle tasks; not only do they provide or extinguish signals by cleaving exterior peptide mediators, but they also may function as receptors or participate in signal transduction or in adhesion. Dipeptidyl peptidase IV (**DPPIV**), which is identical to the lymphocyte surface glycoprotein CD26, is unique among these peptidases because of its ability to liberate Xaa-Pro and less efficiently Xaa-Ala dipeptides from the N-terminus of regulatory peptides. It occurs in the plasma membrane as a homodimer with a total molecular mass of 22-240 KdA and the C-terminal domain probably forms on alpha/beta hydrolase fold. In **addition** to, but independent of its serine type catalytic activity, **DPPIV** binds closely to the soluble extracellular enzyme adenosine deaminase. The in vivo expression on epithelial, endothelial and lymphoid cells of **DPPIV** is compatible with a role as physiological regulator of a number of peptides that serve as biochemical reporters between and within

the immune and neuroendocrine system. Surprisingly, not cytokines with a N-terminal Xaa-Pro motif, but a number of chemokines have recently been identified as substrates. Despite **DPPIV** mediates only a minimal N-terminal truncation, important alterations in chemokine activities and receptor specificitIes were observed in vitro together with modified inflammatory and antiviral responses. Most probably the great flexibility of the N-terminus of a number of chemokines facilitates the accessibIlity to the catalytic site of **DPPIV**. Other known substrates which are subject in vitro to receptor-specific changes induced by **DPPIV** truncation include neuropeptides such as substance P, peptidE YY and neuropeptide Y. On the other hand, **DPPIV** mediated cleavage of the N-terminal His-Ala or Tyr-Ala dipeptides from circulating incretin hormones like, glucagon-like peptides (GLP)-1 and -2, gastric inhibitory polypeptide (GIP), all members of the enteroglucagon/GRF superfamily, results in their biological inactivation in vitro and in vivo. Administration of specific **DPPIV** inhibitors closes this pathway of incretin degradation and greatly enhances insulin secretion. The improved glucose tolerance in several animal models for type II diabetes points to specific **DPPIV** inhibition as a pharmaceutical approach for type 2 diabetes drug development.

L2 ANSWER 9 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2000161978 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10698152
TITLE: Good or evil: CD26 and HIV infection.
AUTHOR: Ohtsuki T; Tsuda H; Morimoto C
CORPORATE SOURCE: Department of Clinical Immunology and AIDS Research Center, The Institute of Medical Science, The University of Tokyo, Japan.
CONTRACT NUMBER: AI29530 (NIAID)
AR33713 (NIAMS)
SOURCE: Journal of dermatological science, (2000 Apr) 22 (3) 152-60. Ref: 62
Journal code: 9011485. ISSN: 0923-1811.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000330

AB Acquired immune deficiency syndrome (AIDS) is an incurable disease at present and so many efforts to conquer this disease are being made around the world. In studies of human immunodeficiency virus (HIV) infection and the disease progression, it has been reported that T cells expressing CD26 are preferentially infected and depleted in HIV-infected individuals. CD26 is a widely distributed 110 kDa cell-surface glycoprotein with known dipeptidyl peptidase IV (**DPPIV**) activity in its extracellular domain. This ectoenzyme is capable of cleaving N-terminal dipeptides from polypeptides with either proline or alanine residues in the penultimate position. On human T cells, CD26 exhibits the co-stimulatory function and plays an important role in immune response via its ability to bind adenosine deaminase (ADA) and association with CD45. Recent studies have been stripping the veil from over the relationship between CD26 and HIV infection. Susceptibility of cells to HIV infection is correlated with CD26 expression, and HIV transactivator Tat and envelope protein gp120 are reported to interact with CD26. These observations indicate that CD26 is closely involved in HIV cell entry and that CD26-mediated T cell immune response is suppressed. In addition, it has been demonstrated that the anti-HIV and chemotactic activities of RANTES (regulated on activation, normal T cell expressed and secreted) and stromal cell-derived factor-1 (SDF-1) are controlled with the **DPPIV** activity of CD26. Thus, the regulation of the function of chemokines by CD26/**DPPIV** appears to be essential for lymphocyte trafficking and infectivity of HIV strains.

L2 ANSWER 10 OF 13 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2000050591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10583373
TITLE: Binding to human dipeptidyl peptidase IV by adenosine deaminase and antibodies that inhibit ligand binding involves overlapping, discontinuous sites on a predicted beta propeller domain.
AUTHOR: Abbott C A; McCaughan G W; Levy M T; Church W B; Gorrell M D
CORPORATE SOURCE: A.W. Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Centenary Institute of Cancer Medicine, University of Sydney, Australia.
SOURCE: European journal of biochemistry / FEBS, (1999 Dec) 266 (3) 798-810.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000131

AB Dipeptidyl peptidase IV (DPPIV) is an atypical serine protease that modifies the biological activities of certain chemokines and neuropeptides. In addition, human DPPIV, also known as the T-cell activation antigen CD26, binds adenosine deaminase (ADA) to the T-cell surface, thus protecting the T-cell from adenosine-mediated inhibition of proliferation. Mutations were engineered into DPPIV (five point, 16 single point and six deletion mutations) to examine the binding of ADA and 19 monoclonal antibodies. Deletions of C-terminal residues from the 738-residue extracellular portion of DPPIV showed that the 214 residues C-terminal to Ser552 were not required for ADA binding and that peptidase activity could be ablated by deletion of 20 residues from the C-terminus. Point mutations at either of two locations, Leu294 and Val341, ablated ADA binding. Binding by six anti-DPPIV antibodies that inhibited ADA binding was found to require Leu340 to Arg343 and Thr440/Lys441 but not the 214 residues C-terminal to Ser552. The 13 other antibodies studied bound to a truncated DPPIV consisting of amino acids 1-356. Therefore, the binding sites on DPPIV of ADA and antibodies that inhibit ADA binding are discontinuous and overlapping. Moreover, the 47 and 97 residue spacing of amino acids in these binding sites concords with their location on a beta propeller fold consisting of repeated beta sheets of about 50 amino acids.

L2 ANSWER 11 OF 13 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1999236842 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10221653
TITLE: CD26/dipeptidyl peptidase IV differentially regulates the chemotaxis of T cells and monocytes toward RANTES: possible mechanism for the switch from innate to acquired immune response.
AUTHOR: Iwata S; Yamaguchi N; Munakata Y; Ikushima H; Lee J F; Hosono O; Schlossman S F; Morimoto C
CORPORATE SOURCE: Dana-Farber Cancer Institute, and Department of Medicine, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: AI12069 (NIAID)
AI29530 (NIAID)
AR33713 (NIAMS)
SOURCE: International immunology, (1999 Mar) 11 (3) 417-26.
Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 19990714

Entered Medline: 19990629

AB CD26, a 110 kDa cell surface glycoprotein, exhibits dipeptidyl peptidase IV (DPPIV; EC 3.4.14.5) enzyme activity and plays an important role in T cell co-stimulation. In the present study, the function of CD26/DPPIV in transendothelial migration was examined using beta-chemokines as chemoattractants. When soluble recombinant CD26 (sCD26/DPPIV+) was added to the transendothelial chemotaxis system, chemotactic migration of T cells toward RANTES was significantly enhanced. Addition of sCD26 to 50 ng/ml of RANTES enhanced the migratory response by a factor of two compared to RANTES alone, whereas mutant soluble CD26 (mCD26), lacking the DPPIV enzyme activity, had no enhancing effect on RANTES-induced T cell migration. In the process of analyzing the mechanisms of the enhancement of T cell migration by sCD26, we showed that RANTES was cleaved by sCD26 under physiologic conditions at the precise site characteristic of its enzyme specificity. However, synthesized RANTES which lacks two N-terminal amino acids showed a chemotactic activity equivalent to full-length RANTES on T cells. Furthermore, addition of sCD26 showed enhancement of T cell migration induced by both forms of RANTES. In contrast to T cells, the truncated RANTES is inactive in chemotaxis of purified monocytes and supplement of sCD26 but not mCD26 reduced the migratory response of monocytes to RANTES. These results suggest that CD26/DPPIV differentially regulate the chemotactic response of T cells and monocytes to RANTES.

L2 ANSWER 12 OF 13 MEDLINE on STN
ACCESSION NUMBER: 97326822 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9183643
TITLE: Role of CD26 for CD4 memory T cell function and activation.
AUTHOR: Dong R P; Morimoto C
CORPORATE SOURCE: Division of Tumor Immunology, Dana-Farber Cancer Institute, USA.
CONTRACT NUMBER: AI29530 (NIAID)
AR33713 (NIAMS)
CA55601 (NCI)
SOURCE: Human cell : official journal of Human Cell Research Society, (1996 Sep) 9 (3) 153-62. Ref: 47
Journal code: 8912329. ISSN: 0914-7470.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970718

AB CD26 is a 110 kDa T cell activation antigen and has been shown to have DPPIV enzyme activity which cleaves amino-terminal dipeptides with either L-proline or L-alanine at the penultimate position. Recent studies showed that CD26 plays an integral role in T cell activation. A partial explanation of the mechanism of CD26 mediated T cell signaling appears to be its association with CD45 tyrosine phosphatase, which may be importance in T cell activation and signal transduction. In addition, we showed that CD26 is a receptor for adenosine deaminase (ADA). Moreover, ADA on the cell surface is involved in an important immunoregulatory mechanism by which released ADA binds to cell surface CD26 and this complex is capable of reducing the local concentration of adenosine. Thus, CD26 is a multifunctional molecule controlling many key aspects of lymphocyte function.

L2 ANSWER 13 OF 13 EMBASE
on STN
ACCESSION NUMBER: 95364261 EMBASE
DOCUMENT NUMBER: 1995364261
TITLE: Is CD26/dipeptidyl peptidase IV a really important molecule in T cell activation of a certain rat strain?.
AUTHOR: Iwaki-Egawa S.; Watanabe Y.; Fujimoto Y.
CORPORATE SOURCE: Department of Clinical Biochemistry, Institute of

Pharmaceutical Sciences, 7-1 Katsuraoka-cho,Otaru,
Hokkaido, 047-02, Japan
SOURCE: Immunobiology, (1995) Vol. 194, No. 4-5, pp. 429-442.
ISSN: 0171-2985 CODEN: ZIMMDO
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 951228
Last Updated on STN: 951228
AB A new monoclonal antibody (MS-7 mAb) was raised to investigate the real role of the membrane-associated molecule CD26/dipeptidyl peptidase IV (DPP IV; EC 3.4.14.5), which transduces activation signals in T cells. A strain of rats which is deficient in DPP IV was used. MS-7 mAb recognized DPP IV (110 kDa) and its 60 kDa fragment, starting at the 281st residue corresponding to the extracellular one comprising the active-site sequence Gly-X-Ser631-X-Gly of DPP IV. MS-7 mAb recognized CD26 on T cells of DPP IV+ rats both before and after mitogen activation. CD26 expression and DPP IV enzyme activity are increased on T cells following their activation; nevertheless, no CD26 was expressed on T cells of DPPIV- rats, and no DPPIV enzyme activity was detected either before or after mitogen activation. In addition, MS-7 mAb inhibited the mitogen-stimulated proliferation of DPPIV+ rats, but did not affect that of DPPIV- rats. These results suggest that CD26/DPPIV is not a necessary molecule in T cell activation, and that there is some other bypass in T cell activation of DPPIV- rats.